In the claims:

1-22. (cancelled).

23. (currently amended) A method of modifying the electrophysiological function of an excitable tissue region of an individual, the method comprising:

(a) providing cells expressing at least one polypeptide forming a functional ion channel or transporter and at least one polypeptide forming gap junctions; and

(b) -implanting said cells into the excitable tissue region, ~~wherein~~ such that each implanted cell forms:

(~~a~~i) gap junctions with at least one cell of the excitable tissue region; and

(~~b~~ii) a functional ion channel or transporter;

thereby modifying the electrophysiological function of the excitable tissue region.

24. (original) The method of claim 23, wherein said ion channel is selected from the group consisting of a sodium ion channel, a potassium ion channel, a calcium ion channel and a chloride ion channel.

25-26. (cancelled).

27. (currently amended) The method of claim ~~25~~38, wherein expression of each of said at least one polypeptide from said exogenous polynucleotide is regulatable by an endogenous or an exogenous factor.

28. (original) The method of claim 23, wherein an ion permeability of said functional ion channel is regulatable by an endogenous or an exogenous factor.

29. (original) The method of claim 23, further comprising the step of regulating permeability of said functional ion channel or an activity of said transporter to thereby regulate the electrophysiological function of the excitable tissue region.

30. (currently amended) The method of claim ~~28~~29, wherein said step of regulating said permeability is effected by administering said exogenous factor to the excitable tissue region.

31. (currently amended) The method of claim 23, wherein each implanted cell ~~is capable of forming~~forms said functional ion channel or transporter following induction.

32. (original) The method of claim 23, wherein the excitable tissue region forms a part of an organ selected from the group consisting of a heart, a pancreas, a kidney, a brain and a liver.

33. (original) The method of claim 23, wherein the method is utilized for regulating cardiac arrhythmia.

34. (original) The method of claim 23, wherein the method is utilized for regulating secretion of endogenous factors from an organ including the excitable tissue region of the individual..

35. (original) The method of claim 23, wherein the method is utilized for regulating neuronal discharge.

36. (currently amended) A method of modifying the electrophysiological function of an excitable tissue region of an individual, the method comprising:

~~the step of expressing an exogenous polypeptide in at least a portion of cells forming a part of, or being in contact with, the excitable tissue region, said exogenous polypeptide being capable of forming a functional ion channel or transporter within said at least a portion of said cells to thereby modify the electrophysiological function of the excitable tissue region.~~

(a) transforming cells with an exogenous polynucleotide encoding at least one polypeptide forming a functional ion channel or transporter and/or

at least one polypeptide forming gap junctions; and

(b) implanting said cells into the excitable tissue region of the individual, such that each implanted cell forms:

(i) gap junctions with at least one cell of the excitable tissue region; and

(ii) a functional ion channel or transporter;

thereby modifying the electrophysiological function of the excitable tissue region of the individual.

37. (cancelled).

38. (new) The method of claim 23, wherein each of said at least one polypeptide forming said functional ion channel or transporter and at least one polypeptide forming gap junctions is expressed from an exogenous polynucleotide.

39. (new) The method of claim 23, wherein each of said at least one polypeptide forming said functional ion channel or transporter and at least one polypeptide forming gap junctions is expressed from an endogenous polynucleotide.

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-37 are in this case. By the Office Action dated May 15, Claims 1-22 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 23-37 have been rejected. Claims 1-22, 25-26 and 37 have now been canceled. Claims 23, 27, 31 and 37 have now been amended. Claims 38 and 39 have now been added.

Applicant filed a response to the Office action on August 14, 2003. In an Advisory Action dated September 26, 2003 the Examiner indicated several errors in the format of this response and refused the entry of the amendment. The present response addresses and corrects all those issues.

35 U.S.C. § 112, First Paragraph, Rejections

The Examiner has rejected claims 23-37 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner points out that the specification, while being enabling for implantation of unmodified cells and *ex-vivo* gene transfer, wherein the implanted cell is transformed prior to transplantation, does not reasonably provide enablement for *in vivo* gene transfer, wherein the implanted cell is transformed following implantation.

While traversing the above rejection, Applicants, in order to expedite prosecution of this application and obtain an early issuance thereof, have amended claims 23 and 36 to overcome this rejection in the manner suggested by the Examiner, and put them in allowable condition by restricting the claimed invention to *ex-vivo* gene transfer.

Thus, claim 23 has now been amended to recite:

23. A method of modifying the electrophysiological function of an excitable tissue region of an individual, the method comprising:

(a) providing cells expressing at least one polypeptide forming a functional ion channel or transporter and at least one polypeptide forming gap

junctions; and

(b) implanting said cells into the excitable tissue region, such that each implanted cell forms:

(i) gap junctions with at least one cell of the excitable tissue region; and

(ii) a functional ion channel or transporter;

thereby modifying the electrophysiological function of the excitable tissue region. (Emphasis added).

Claim 36 has now been amended to recite:

36. A method of modifying the electrophysiological function of an excitable tissue region of an individual, the method comprising:

(a) transforming cells with an exogenous polynucleotide encoding at least one polypeptide forming a functional ion channel or transporter and/or at least one polypeptide forming gap junctions; and

(b) implanting said cells into the excitable tissue region of the individual, such that each implanted cell forms:

(i) gap junctions with at least one cell of the excitable tissue region; and

(ii) a functional ion channel or transporter;

thereby modifying the electrophysiological function of the excitable tissue region of the individual. (Emphasis added).

In view of the above amendments, the Examiner's rejections of claims 23-37 under 35 U.S.C. § 112 first paragraph, is deemed to have been overcome, and the withdrawal of this rejection is deemed to be in order.

35 U.S.C. § 112, Second Paragraph, Rejections

The Examiner has rejected claims 25-27, 31 and 37 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

By this amendment, Claims 25-26 and 37 have been canceled, rendering moot the Examiner's rejection. Claim 27 now depends from new claim 38. Claims 31 and 36 have been amended.

With respect to claims 31 and 36, the Examiner points out that these claims are indefinite in their recitation of "capable of", which is merely a potential property and not an actual property.

Claims 31 and 36 have been amended to no longer include the phrase "capable of", to thereby overcome the Examiner's rejection with respect to this claim. Claims 25-26 and 37 have now been cancelled.

New claims 38 and 39 have been added, and depend from allowable claim 23, and their allowance is respectfully requested.

In view of the foregoing amendments and remarks, it is respectfully submitted that claims 23, 24, 27-36 and 38-39 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited. Should any outstanding issues need clarification to put the application in condition for allowance, the Examiner is invited to leave a message on the voice mail of 703.415.1581.

Respectfully submitted,

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Date: October 1, 2003.